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- 6) Documents cited
 Nature 1982, 299, 178-
- B) Field of search
- 1) Applicant Annual Research

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(54) Genetic engineering

(57) It has been a problem to find an alternative, less time-consuming, and more reliable source of factor IX, a polypeptide which is essential to the human blood-clotting process and necessary for the treatment of patients with Christmas disease. In order to aid in the solution of the problem, there is provided recombinant DNA containing a DNA sequence occurring in the human factor IX genome, and includes recombinant DNA comprising substantially the whole sequence of human factor IX genome, which is

inserted in a cloning vehicle a transformed into a host, such Escherichia coli. Other fragme the sequence have also been and the invention includes DN molecules comprising part or human factor IX DNA. There is described cDNA derived from factor IX RNA. Uses include th provision of an intermediate o in the genetic engineering of a IX polypeptide precursor and t manufacture of the factor IX polypeptide, and in making pr use in diagnosing the presencnormal or abnormal factor IX' patients with Christmas disea

of the so nan lue stor nce s for

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1st amino acid
sequence:

Glu-Cys-Trp-Cys-Gln-Ala

5' GA_G^A UG_C^U UGG UG_C^U CA_G^A GCN 3'

Deoxyoligonucleotides 3' CT_C^T AC_G^A ACC AC_G^A GTT CG (oligo N2A)
synthesized:

3' CT_C^T AC_G^A ACC AC_G^A GTC CG (oligo N2B)

2nd amino acid
sequence:

His-Met-Phe-Cys-Ala

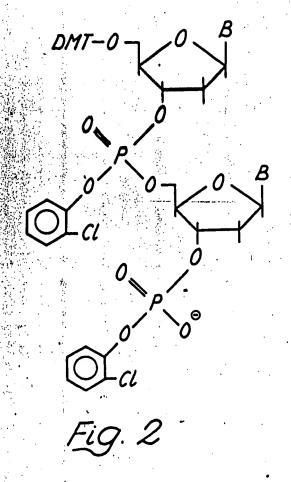
mRNA:

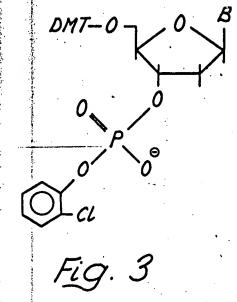
5' CA_C^U AUG UU_C^U UG_C^U GCN 3'

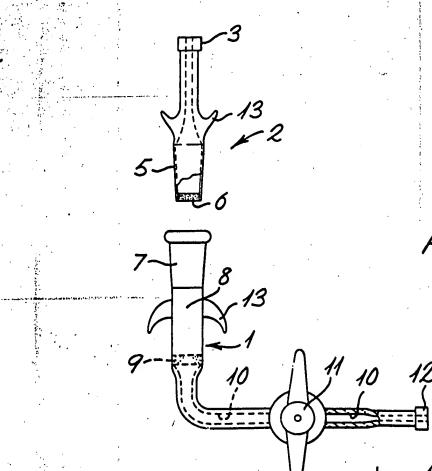
Deoxyoligonucleotides
synthesized:

GT_G^A TAC AA_G^A AC_G^A CG (oligo N1)

Fig. 1







60 SNPCLNGGMCXDDINSY TGAATCCAATCCATGTTTAAATGGCGGCATGTGCAAGGATGACATTAATTCCTAT : 10 30 70 E C W C Q A G F E G T N C E L D A **GAATGTTGGTGTCAAGC**TGGATTTGAAGGAACGAACTGTGAATTAGATGCAACATGCAGCATTAA 90 100 110 120 80 100 NG CKQFCKRDTDNKVVC GAATGGCAGATGCAAGCAGTTTTGTAAAAGGGACACAGATAACAAGGTGGTTTGT 130 140 · 150 160 120 110 S C T D G Y R L A E D Q K S C E P A V P F P TCCTGTACTGACGGATACCGACTTGCAGAAGACCAAAAGTCCTGCGAACCAGCAGTGCCATTTCC 220 180 190 200 210 230 140 150 C G R V S V S H [V R P R F H G L C S C * E CTGTGGACGAGTCTCTGTCTCACATGTGAGGCCCCGCTTTCACGGTCTGTGTTCGTGCTGAGAA 270 250 260 280 290 300

Fig. 5

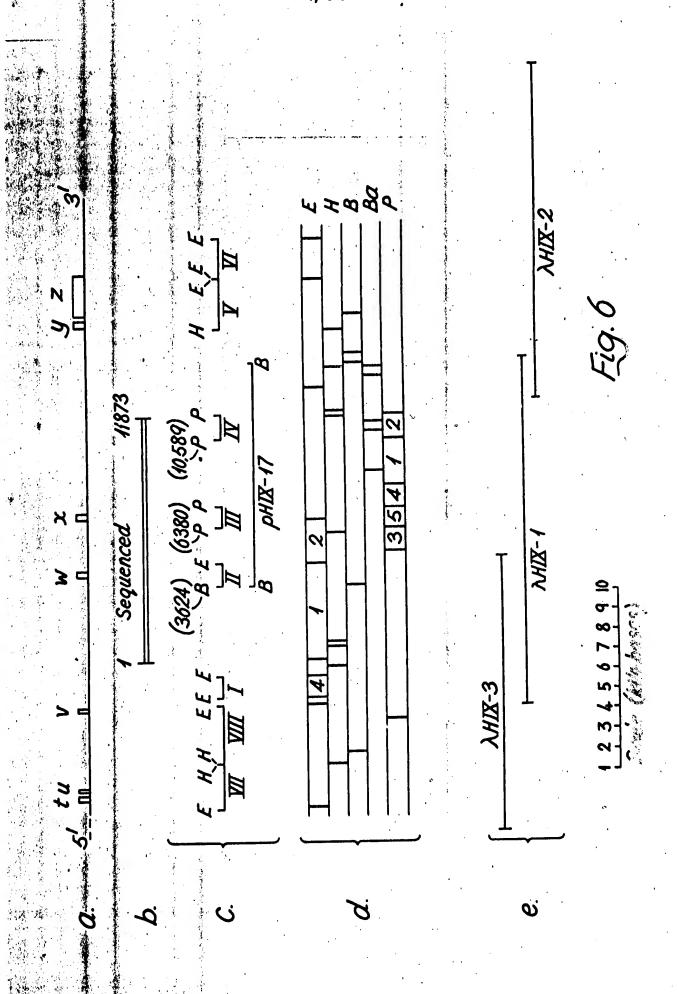


FIG. 7a		• •	•							
rcctagttggatatgcttgggtacagagggt-atagtascattactgggtca-gcatsaacagggaagctttca 1610 1020 1030 1040 1050 1060 1050 1050	ACTGCCTCA-GCA 0 1080	1050t	GGT-ATAGTAS(TGGGT ACAGAG	1020 1020	ATTTCCTAGT 1610	.C.T.CC.T.C.A.C 1C00	GGGAATTAA 990	TTCGACTTAT 980	TCATTGGTTAGA4STTCGACTTATGGGGAATTAACTC-CTCACATTI
TICTAACAGCAACTGATTGCTTAACTTCCTAGGAC TGTCTCCAATAAGTCAAATTG-CCTCAGGTTAGCCACCTGAGGAAGGGAGGAATTTGTCTGTC	STGAAGGATTTG O 940	9308	GAGTGGAAAGAA 920	STTAGCCACCT 910	TTG-CCTCAG(ATAAGTCAAA 390	CTGTCTCCA 880	CTTCCTAGGA 870	GATTGCTTAA BOÜ	TTCTAACAGCAACT 850
AAAAAAGTCACAAGCTTATTTAACATGTGCAATCCCA-GGSSCAAGAGAACTGAAGAGGCAGGAAGGAAAGGAAAG-CAATAAGAGGATGAGTTATCAAACTACTCGT 730 740 810 820 830 830 840	AATAAGAGGATG B20	1AG-(AAAGGAAAAGAA 300	34 5 T GAGGCAG 790	AGGAACTGAAG 789	55CA 25 26 23.	ATCCCA-66 700	44C4TGTGCA 750	CITATITATT. 740	AAAAAGTCACAAG 730
TTATTACATTIG-TCATGICATATATGIAAAATAGAGITTAAAAGITTAGATTCATCACTCATATTCTCCAAAACCATACAGTCACTCTGTTAGCCTGTGTTCCCCCAGA 813 026 630 700 710 720	.AGTCACTCTGTT) 700	ATA(TTCTCCAAAACC 683	MAAATTCATA 673	FTCATCACTCA 660	AAAGIITAGA 650	TAGAĞTTTA 649	ATATGTAAAA 630	C AT GT C A G C T	ITATTACATTTS-TI 513
TCATSCCCTTASTGAATTATTSGT4SCAAASGTTAAAGCTCAAGCTGSTTCCTTTGTCCCTG-CAACAGTTGATTT-CCTCCTTTATCTCCTGAAGTACCGTAAG-ACTAAGAGCCAA 490 500 500 500 510 520 530 540 540 600	TCCTGAAGTACC	TATC 570	111-CCTCCCTT 560	CAACAGTTGA 550	77GTCCCCTG- 549	6CTGSTTCCT) 530	A A GCTCAA S 2 0	AGCAAAGGTT 510	8 AT 1 A 1 T 5 G T . 50 3	TC.2.T.S.C.C.C.T.A.S.T.G.I.
TJGCAACAJATIGCT GCTACCAGAAAAGTTCAGGAATATTACCACTGTTAGTGAGGAAAGGCCTTTTAATTAA	ATTAATAGAACC		ATTAATTAATTA 440	430	16TGAGSAGAA 420	TACCACTGTT!	C A GG A A T A T 4 3 0	CAGAAAGTT 390	7 46CT 46T A A (T16 C46C4114 TG-
ACAATCTCATATTGACGGAACACTTTCTACAGGTAATGTTTAGCTTGGCTGAACACTTTAGCAATTGCTTCTG 290 300 310 320 330 340 350 360	TTTGGCTGACA(11AG	TACAGGTAATGT 320	GAACACTTTC 310	CATATTGACG 300	TATCACAATC1 290	TTCGTAACT 220	16CT6CaCCT 273	rsaca aageal 20u	CATTSTGCATGCCCTSACAAGCAAGCTGCACCTTTCGTAACTTATC 250 270 280
CAGCAGCAACATACTGAGCCCTAAAS-GGTGACAAAT\$TSGASAATGATACAGAGGTCTGGTTACTTCTTAGCCAAATGAGAAATGAGAAAAGAGAGAG	AATTGAGAAAAC.	7CAC 210	AATGACACAGAA 200	CTTCTTAGCC.	165TCTGGTTA 180	AATGATACAGI 170	AATETSGAS TeO	15-66TG4CA	I GASCCCTAA:	CAGCAGCAACATAC
GAETTECTTSTECCATATTTTTSTEGAATCTTCASCCTTTTAGCTGAAAGATTGCTGATTSGAAGCAATTTCCCACCTCCTGGGAAACAAGAAGAAGAAGAAGAAGA 10 10 20 20 10 10 20 30 40 50 50 60 60 70 70 80 90 90 100 100 110 120	TCCTGCGCAAAA 100	0	AGCAATATTCC 90	CTGAT1 36A/ 70	.CAAAGATTG 60	11 A G C T G A 3 G G S û	TTCASCCTT +0	11CTGGAATC 30	LTETTTATI 2C	6aa TTCC T15T GCC. 10

FIG. 7a

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AATTTATATTCATAACTTGCAGAAGCAAAATTTCTTAAAATACAAAA 3370 3360 3360 341	ACACTACTTCGACTGAAAAGACAAGTCACAGAGTGAGAGATATCTG ACACTACTTCGACTGAAAAGACAAGTCACAGAGTGAGATATCTG 3530 3530 3530 3530	AAATTGCTTGGCAGTAATCTAGATCTGAACATGTGATCCAGTAATT 3610 3620 3530 3640 355	Cactattatacataa sagccaaaaactsgaaacaa accaaatatccatt 3739 3740 3750 3769	ACT GCTGTACA AAC AACATGGTTTAATCTCACAG ACAAAATGTTAAA1 3850 3860 3870 3880 383	GTTASAAGTCCAGUTAATGGTAACCTATAAAAAGGAAAAGGGTGGAAT 3970 3990 3990 4000	TCATTTACTTTSTGE MAACTTECACTABMATTGTGTGTTTTTTTTGAAT 400 4120 4120 4130	CATTIAGITITA A CCAATCAAT TATAGIGCIACCAICATITITA ISCATIATIGAS A A 270 4280 4280 4290 4250 4300 4310 4320 4320	TATISGGGGGAACATGAATGCCCCCCAATGATTTGACCCCATACATGAGTTCCATSTACTTTTAGAAATGCATGTTAAATGCTGTTACTGTCTATTTTGCTTCTTTT 4350 4340 4350 4350 4350 4370 4370 4380 4390 4400 4410 4420 4430 4430	F C N I N S R C ≡ G F C K N S A D N K V V C S C T E G V R L A E N Q K S C C I E G V R L A E N Q C C C C C C C C C C C C C C C C C C	,
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FIG. 7e

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25.5	ATATC • 690	310	56CT1	ATSA1 5050	6151 <i>1</i> 5170	265	ACT.	A AG 5 30	T 44, 559
A C	1 A A .	77.	146.	. 44. S.	7 A G:	S A S	ASC S	ATG	- 444 S
GAACCASCASTCATAATCTGAATAAGATTTTTTAAAGAAATCTGTATCTGAAACTTCAGCATTTTAACAAACCTACATAA1 4570 4680 4690 4600 4600 4610 4620 4639 4640	TAGAAAATATCAGTAGCTTGAATTAGACCAATTAATTTTCTAGATTGCA 4690 4700 4710 4720 473	TITCICTAACATITATATCACAAATAAATTIGIGIGATTICIGCATAIGIATITGTAATTCAICAAGTCAATGTAGTAATACTATATCATAAAATATACACAAATAATGA 4810 4820 4830 4840 4350 4860. 4870 4880 4890 4900 4900	GTGATAGGCTTCTAGTATAAGGACGGTAAGTTTGAAGCATGATTCTATC 4930 4940 4950 4950	GT CASAATSAT TCCG GC AA TGAACTGTTTTATGTT CTGCTAGGCTGA TC SOSO SOGO SOGO SOGO	TGATTAGTSTATTCAGAACATCTCCACTCCATGTTCGTATGGCTGTTA S170 S170 S170	4AA TGAGGGC TTTT TT UA AGGAAAC TAGATATAA TTTCTTTTGC 4TTT 5290 5330 5330	TCT CAGCACTATACCAGAAGAAATTAAAGAAAAAAAAAGAACCAGTGC CGAGATCGTTGGTC AGGGAGACCTTACGGGGATTTAAAGACACACACACAGAAATATA 8410 8420 8420 8430 8440 8450 8450 8460 8470 8480 8490 8590	GASTATGAAGTGSGAJATCAGGGGTCTCACAGCCTGAGAGCCCCGAACAGAGÁTTACCCACATATTTATTGACAGCCAGTCATAAGATTTACTGAAAGTATTCCTTA 5530 5540 5550 5550 5530 5570 5580 5590 5600 5610 5620 5620 5630	TGGGAAATAAA GGGATGAGTGGTGGTATTTGCAGCAGGAACATGTCCTTAAGGCACAATTGTTGCAATTGTCTGTGGTTTAAGAACACCTTTAAGCAGTTTTCCGCCCTGGG 5659 5560 5560 5670 5630 5690 5709 5710 5720 5730 5740 5750
5	₹ .	Ħ	<i>)</i>	5	. 2	r a	7	3	1

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OZSO 6250 6270 5280 6290 6310 6320 6320 6350 5260 5350 6250 520 6350 520 6350 520 6350 6350 6350 6350 6250 6250	
5 1 T A C A	
6413	0079
GAAAA1 OS3	TTATTITICITIAGAAAATAA2CCAACCCAAGGAAAAATGGTGGGCAGGTCCTGGTGAATATGGCTGTGATAATTATTAGCAATCTCT

AATACA AAATTAGCTAGGTGTGATGACTCCTGTGCTCCCAGCTATICAGGGGGGGGGG	8020 8020	54CTCCCAC 5010	CTAGGTGTGA1 8000	10	970 7980 970	- ~	0-06 A A C C C C C C C C C C C C C C C C C	765-CA3CAC 7950	7940 7940	TAACCGA-ATTTGA-AAC-CCTGG-CAACACG-CGAACCCCACCTC 79130 7940 7950 7960
7910 7920	2900	0.687	7880	7870	7860	7 350	0762	16TTCTC6T- 7830	7320 7320	46.8 GTCTTGATCTAC CACT ATAGTTCTCGT-7830
	7730	1 TAAGGCAAG	15646644664 7750	14665ACTCA4 7750	.665T AAA6AA 7740	atttaaaasgggst4 7730	AAAT T GGATT 7729	166CT A A G A A A 7 7 1 9	. AA A GT CT TT 4 7700	GGT GAGAGTTG GAAA GTCTTTAGGCT AAGAAAATTGGATTATTTA. 7590 7719 7729
CATSAASSTCTGSAAGAAGGTCGCAGGTACTCAGGCCACTACTTCAGCTTCAGCCCTTGCAAAACT	CTACTTCAG 7660	GTTCAGGGCA 7650	JAGGTACTCAG 7640	GA AAGGTCGC 7630	ASSTCT65AA 7520	AACAACATSA 7613	3C465TC 7600	.TCCAGACAG	. 47 & GC & G & G & 4 T S 8 O	TAAGSAAACAGCATAGCAGSATTCCAGACAGSCAGGTCAACAAG
CCTC CAGAGATGAGCAGTGGAGAGAGGGCT CAAACCAGCTACCATACAGGTCAAGAAGAATTTGGCAT 490 7500 7510 7520 7530 7560	.TACCATACA 7549	CAAAACCAGC 7530	IAAGAGAGGCT 7520	CA GTTGGTGA 7510	CAGAGATGAG 7500	AG AAGGCCTC 7490	1 A C C À A T G T G 7 4 3 0	TTCAGCACT	TTA 56CA 46T 746C	TGTGASABGTATTTASGCAAGTTTCAGCACTAACCÂATGTGAGAAGG
AACTGGAGCTCAGCTGGCCAGGTGGGAGACTGAGGCTATTTTACTAGACAGAC	66CTATTT 7420	GGGAGACTGA 7410	.ca66CCA66T 7400	TG GC A A G A C A 7 3 9 0	66 a G C T C A S C 7 3 8 0		CTGATGGTG 7360	GTACTTTAT	CCCTTSGCAS 7340	P
N I T Q S T Q S F N D F T R V V G G E D A K acatcactcaaagcacccaatcatttaatgacttcactcgggttgttgstggagaagatgccaa 7260 7270 7280 7290 7300 7310 7320	ACTCGGGTT(N D F TAATGACTTC 7290	T 2 S F CCCAATCATT 7280	T 0 S AC TC A A G C A 7270	I L D N I TTTTSGATAACATC	E T I L AAACCATTTT 7250	T E A E CTGAAGCTGA 7240	V N S GTAAATTCTA 7230	V 3 V TGT 5GACTAT 722G	V F P D V D V N S T E A E T TGTTTCCGAGCTGAACCA 7210 7210 7226 7230 7240 7
TTCTAAGCTCACCGTGCTGAGGC 7180 7190	A A A	S V S CITCTETTCAC	V P F P C G R V TITTCTAGTGCCATTCCATGTGGAGGGTTT 7150 7169	CCATTCCAT	V TTTTCTAGTG	CT41	TTACTAATT1 7120	ABATATCAGG 7113	TGC CAAT 3AS. 710G	ACATSTECCATTIGC CAAT SASABATATCASGTTACTAATTTTTCTT 7090 7100 7110 7120
SCTTCTCAGAAGTGACAAGGATGGGCCTCAATCTCAATTTTTGTAAT. 7040 7050 7060 7060 7070	364T566CCT 7000	SAGTGACAA(C SCTTCTCA(AAATAC TGATGGGCC 920 7030	711111881/ 7920	TGATTEGET	CTCTATTCAC 7000	745CTTGAGA 6990	ATCAACCTTT1 6780	SAAAATAACSCAATCAACCTTTTASCTTGAGACTCTATTCACTGATT
GICATTAGACTCT3TAAAGTCTTACCAAATTTGATTCTGGAACACCTATTTCCGTAAAGATGATGAATTCCGGAGCCAAATGTTCTTTTCATGAAGGATTTGAAAACTGTCCAT 61CATTAGACTCT3TAAAGTCTTACCAAATTTGATTTCTGTTTTCTATTTCCGTAAAGATGATGATGATGTTCTTTTCATGAAGGATTTGAAAACTGTCCAT 6950 630 630 630 6970 8830 6290 5900 6910 6910	1TTTCATGAA 6940	AGCCAAATGTTC1 0 6930	4ATTCCGGAGC 5920	0910 0910	.TATTCCGT4	ACACCTATTC 0290	752 TTC 766A 5830	174CCA44TT 087D	CTCTSTAAAGTCTTACCAAA	61CATTAGACTC1

7h	FIG.						•				
	9230	0226	9210	9209	9190	9180	9170	010	9150	0,416	3150
TCATAAATG	TCTTATAAC	AAAAGACAATATTTGCTG-ACCGATCTTATAACTCA	AGACAATATT	AA		1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1		0 0 0 1	1		
9120	9110	9100	0606	0806	9070	9000	0506	670¢	9030	n20o	3010
0006	8990	0868	8970	0968	8950	0768	08.430	8920	8910	6048	Cr 6 S
	8870	8860	8850	0788	8930	3820	0. 0.	00%	8760	8780	6770
0928	8750	8740	8730	8720	8710	390 3700 8710 8720 8730 874		3680	6670	11.C TALT CE	TAC TGC AGAATITCTALT UGATACTATATATATATATATATATATATATATATATATAT
8640 8640	66 A G A T A G A F A G	TAGTAACTACTGTATTGGAGAGGGGGAGGGGAGATAGA 8630 8610 8620 8630	CTGTATTGGA 8610	-TAGTAACTA 8600	.C.CACATGTGG 8590	TTAAGCACATAACAAC CACATGTG5 570 8530 8590		16CACC 16CC 9560	ATTC-TCAAT 8550	TABABATTCA 8540	ATTAIGAGAAATTAAAAATTCAATTC-TCAATTGCACCTGCCAAATT SSIG 8540 8550 9560 8
.TAACTACA 8520	8510	ATATGTTTAAAT 8500	CACTASCCAC 8490	-CAATAGGTAACCACTAGCCACATATG- 8480 8490 85	1 GTGCTGT-C 8470	GTCCTTATATAAGTT GTGCTGT 450 8470	654 T	CAG CAAGCCA	CCTCCCCAGG S430	CIT 166CCCC	AAT MACCCACCTCTTTGGCCCCCCTCCCCAGGCAGGCAGGCAGG
TGASAAGA 3400	ATTCCSTCTG 8390	TGTAGCAAA ATCTGGGTTGTAACTTAGCCTACAGCTGAGAGATTCCGTCTGTGAGAAG 8340 8350 8350 8370 - 8380 8390 940	CTACAGCTGA 8370	GTAACTTAGC 8360	A ATCT GGGTT 8350		A AG-GCT AC AT1 . 8333	TTTACAACC 932û	ACATTTTCA 8:10	TTACCTATGC 8300	SACATATGTAGAATTACCTATGCACATTTTTCATTTAACAACCAAG-6 8290 8300 8310
AACAACCT 8280	1461C16CA 8270	AATAATGCACTTGTAC CTASTCCTTCCGGGTGCTCTGCASACATTTCTCCAAGCGTAGTCTGCAAAC 210 8220 8230 8240 8250	.TGCASACAT 8250	ccc66516CT(8240	CCTASTCCTT 8230	TGCACTTGTA 9220	CACCAAATAA S210	SSGTTCAAAA S200	ACAGAAGCCG(8190)	152 ACTT 6TT. 818 Û	SCCCMAAGGAAATSAACTTGTTACAGAAGCCGGGGTTCAAAACACCA 8170 8180 8190 8200 8
			***		-					in.	
			A Company of the Comp			The second special is an integral					The second of th
8160		8140	9130	8120	3110	41CACACCACTGCACTTCAGCCTGAGTGCAGTGCAGTGCCCCTTTGCGCGCCCCTTTGCGCGCGC	11616A1CAC 9390	.TGCAGTGAA.	14467C6466C 807)	TG AGCC TGSA	TGGGAGAATCACCTGAGCCTGSAAAGTCGAGGCTGCAGTGAATTGTG
A A G A A A A C A C T G		TOBBABACACACACACAAAAAAAAAAAAAAAAAAAAAAAA			, , , , , , , , , , , , , , , , , , ,				このできることによる、大きないのです		こうなん こうしょうできない

	9480	544C46 9600	9226	76ASCC 9840	67TT 9960		10080	10200	10320	
2000	ACTECTSTANTESCETTETTA-GAACETTIECTGGAACAATCECTETTAAGTGCAAGCACTGTTATTATGCCTTCAATGTATTAATATCCATGTATETATTETCTCTAATTTTGTC	GGATAACATGGTTACAACAAAGATCCTACTTTATGACAATTATCTTCCTTGGGTTTGTGGGACATAGAACAG 530 9540 9550 9560 9570 9580 9590 9600	AAGATAACTTCCGTTTTTAAAAGTCCAAGATTCAGGAGATCAAAACCATCCTGGCTAACATAGTGAAACCCCG osu 9660 9670 9680 9690 9700 9710 9720	TATA GTCCCAGCTACA CGGGAGGCTGAGGCAGGAGAGTGGCGTGAACCGGGGGGGG	AAAAAAAAAAAAGTCCAAGTTTAAAAAAAAAAAAAAAAA		10070	10190	ITTCAAAGCACTTTATCTTTCCAAAGGCAAGAAGCTGAGCTACTTTCCAGAATAGTTSTGAAAGACCCTGTCAT 1250 19260 10270 10289 10290 10300 10310 10320	FIG. 7i
• •	CATGTATCTA1 9460	7CCTTGGGTT1 9580	CATCCTGGCT		.AAAAGGTGT. 9943		10050	10180	CCAGAATAGTT 10300	
	ATTTAATATC 9450	ACAATTATCT 9570	AGATCAAAAC 9690	ATCGCGTGAA 9810	144444444 9930		13050	10170	6AGCTACTTT(10290	
さればない できょうしん アンドラン カンドラング かいかい かんしょう かんかん かいかん かいかん かいかん かいかん かいかん かいかん かいか	CCTTCAATST 9440	CCTACTTTATG 9560 ;	CAAGATTCAGG 9680	6 A G G C A G G A S A 9 8 0 0	CCAAGTTTAA 9920	,	10040	10160	GCAAGAAGCT	
	C 1GTTATTAT0 9430	A ACAAAAGATO 9550	T TT A A A G T C (9670	A CGGGA GGC T(A AAAAAAGT(991 <u>0</u>		10030	10150	CTTCCAAAG 10270	
)))))))	AGTGCAAGCA	ACATGGTTAC 9540	41CTTCCGTT 9660	TCCCAGCTAC 9780	4	6	10020	12140	105CACTTTAT 10260	
でしている。 こうかん はいかい かんかん こうしょうかん こうしょうかん こうしょう	ATCCCTCTTA 9~10	TCCATGGATA 9530	CTAAGAAGAT 905U	GCGCC TATA G 9770	CTCCAAAAAA 9390		. 10010	10130		
7.6.2A	7CC 7GGAACA 9400	GTGTCCAACT 9520	aat a ta t t a s 36.43	6TG 5TG 5CA 5 9760	CAGAGCGAGA 9330		10000	10120	10249 10249	
ののです。 これのできない からない こうしゅう こうしゃ こうしゅう こうしゅう こうしゅう こうしゃ こうしゃ こうしゅう こう こうしゅう こうしゅう こうしゅう こうしゅう こうしゅう こう こうしゅう こうしゅう こうしゅう こうしゅう こうしゅう こうしゅう こう こうしゅう こう こうしゅう こう こうしゅう こう こうしゅう こう こうしゅう こう	TA-SAACCTT 9390	CATTCATTAT 9519	aacccagsag 9630	T746CCC56C 975A	.6CCT65SCGA 9870		C666	10110	CCCTATTCAACCACATGAACAGATTACTGATGTGACAG/ 19210 10220 10230 19249 10	
0070	.TGA CC TTCTT		sesatccaas oolg	12TAC2AAAAB 074G	ACTGCACTCCA 930G	· .	0866	10100	TATTCAACCAC 10220	· .:
0.52.4	CTCTGTAATA1	ATTITGIGITCICATGIATITICATTCATTATGIGTCCAACTTCCAT 94.70 0500 7510 9520 9	TGC TCAGAGTASSGS ATCCAASAACCCAGSASAATATATTASCTAAS 9512 9512 9526 9633	TCTCTTCCJAAAATACAAAATTAGCCCGGGGGGGGGGGGG	GASATCCCSCCACTGCACTCCAGCCTGSSCGACAGAGGGGCTCC— 9850 9870 9300 9870		0200	10090	10210	

	10560	A 8 0	300	920	070	160	5CCA 1280):	520
10日本	CT 60	11CA	10	. 10 10	11	A660	11	AAGG	36676
10.10	AAAC	6161	AGAG	110	IAATG	0.0 A G	TCAC	70000	SATG
10.3	1055	1067	1079	1091	1103	1115	1127	1139	1151
7	ACTO	FAGA	AGAAC	AGAC!	1166	CAGA	5011	CCTC	Ů U U U
270	17CA 0540	0990	A A G A O	0000 0000	AGCA 1020	1140	C A G G	6C T A	1500
	6CAG/	6161 1	CACA.	AAAG	200	CACC	ATTC	6111	
10400 10410 10410 10420 10420 10430 10430 10440	GATT 30	AGCA SO	ATCT 70	14666 190	166TT	7677 30	100 TT	1TCCT 370	16777
104	105	106	107	108 108	ACACA 110	111	113	113	110
9-2-0	ACTAG	ATACT	66TG/	AGAG(6611) 0 0	CATT	0-0	SSTA
1040	1052 1052	1064 1064	AC11	1080 1080	1100	1112	1124	1136	1148
2 2 2		ATA:	ISATC	1191	CACTG	ATTCA	56TC4	3 G A A C	A T G G 4
139C	50 A G G	0630	0750	1643(0870	CAAC 0990	1110	, CTGC 1230	1350	6CC A 1
aisciiaetcottiteaaaakiato 370 - ***** 10390 - ***********************************	ACCATGTCATGGTTAATCTGCAGGGAGGAATACTAGATTTGATTGCAGATCAGACTGCAGCAAACCTGCTG	GAAAACATTATATCTAGCTTTG ATATGAATACTGTTTAGCAGTGTCACCTAGAAAGAGTGTTTCAAAA 1510 10629 10030 10640 10650 10650 10650 10670 10680	TTTAGCCAGGGTGGGAATAAAGTGATCACTTGGTGAAGAATCTCACAAAGAAGAACATAGAGATTCACTT	GTTAJAGAAAAGGTGTAGGTGAGCTGTTTGCAAGAGCCACAAGGGGAAAGGGGAAGACATCTTTGTGGACT 1850 10860 1087C 10880 10890 10900 10940	ISAAA SCCCTTTCCAACCAACCACTGGGTTGGTTACACAGGTTGGGCAGCATTGGGAGCAATGTTGATTG 1970 1098G 1099D 11000 11010 11020 11030 11040	SGSGACAGGGGCTAGA TAGCCCCATTCAGGGAG-GGGCATTTGTTCACCTGGCCAGAGATCAGAGCAGGCTAA 090 11100 11110 11120 11130 11140 11150 11160	CCCCCTAGCACGTATCCCGTCTCGCGTCATTTCTTACCTTATCCAGGGCTTTCACCTCAGCTTGCCA	TTCCCAGGACCCCCTATGGTTCCGGAACGGCGCTGCCCATCCTGTTTGCTACCTCCTAAAGCGC 1330 11340 11350 11360 11370 11380 11390 11400	CCGGACAGGAACGCGTGAGGAAGGAGGTACTTCAGTTTCCCTCCAGGCCGGCGGGTGGGCTCAGA 1450 11460 11470 11480 11490 11500 11510 11520
90	61TA	ATAT 20	1666	16616 360	100 A	3C T AG	37 A T C	340	0000
101 101	103	10¢	CA630	GAAA.	100	A G C G (113	646C	664A
 	CA TG	A A D	TA SC.	TA AAO	A A 3C 0	ن 3 AC 0	CC TA	CC AĞ	5G A CA
1037	1049		1073		1097		1121	1133	1145
11 A T	AGCT	AGTG	1110	r a GT	CC A 11	1676(CCATC	66 T AC	44661
	0 8 9 C	601T(7ATC	4765 0940	ACCT(67 TC 1080	4645 1200	1320	TT AG 1440
1.ce	664 T	166 <i>5</i>	CTT7	AGA A	1016	AGC T	CTAC	1166	A A G G
1 C E	71G7 70	C A 5C 90	110	130	CGAT	14845 170	16 A C C	-CTT6	33)
104	TCAT 104	105	107	103 103	100	110	111	-565-	44610
Catal G	CTCC	AGCA4	TTCA!	GATT(1611		0 0	TCTA
1034	1046	1053 1053	1070	1002	1034	1105 1105	75.TG TC 1118	5 CA A C 1130	1142
	A C C A G	I C AAG	4 C C T T	TAATG	A 5 TT G	r s rc G	G A TCC	599 e ø	-)- 9 9
0330	A G 4A I	6664 0570	1554) 0690	66A61 3813	T 5 A A !	167T)	-CTG(1250	5-C-1
AUTICISCATIGITICICECECCACITOCATICESTICES TATES 103330 TIME 10346 TIME 10356 TIME 10369 TIME 10	AAT GAAAGAAACCAGAATCTCTCCTCATTTGTGGATGGGCCAGCTCC	SACTAAGGCATCAAGAGAAGCAAGCAACAGCTGGGCTTCAGTGGT	TUCTSATSCAACCTTTCTCTTCASAGTTGTTTCTTTTATCTTTCAAA 10690 10700 10710 10720 10	TCATCTGGAGTAATGAACAGATTGAACAAACTAGAAATGGTTAGTCT 13919 10820 10830 10840	TAAGSGTSAAASTTGCAAGCAGGCAAGACGATTCTGACCTCCATTAA 13939 10946 10950 10960	AAC LADIGTII SICGGAATIGTISACTTABABAGC TGTTCTGTKACT	56-aCT-CTGGATCCTGTCCASCTTTGAGACCCTACAGASCCATGT1 11170 11183 11190	GGCTSSAGCCAAGGSCAACGCAGCCGC-CTTGTTCGCGATGGTAGCT 112~3 11300 11310 11320	TGGCGGG-C-GG-CCTTCTAAAGTCGCGCAAGGTTAGAAGGTT(11410 11420 11430 11440 1
4	4	3	₽.	70	=	A	13	3	Ξ,

FIG. 73

0.0011 0.0011 0.0011 0.0011 0.0011 0.0011 0.0011 0.0011 0.0011 0.0011 0.0011 0.0011 0.0011 0.0011 0.0011 0.0011	FACCGCCACGTAGGGAAGGAATGAAAACCTTTGAATATTAGTGAAAAAAGGGAAACTSCAACGCCTGTATTACT 1890 11700 11710 11720 11730 11740 11750 11760	TGCCAGCTG
11620	11740 11740	AS A TAGC TITC A TC A LC AGCTC A AAACC SC CAT TTA AAS CAACACC GCATTITGSCTT TC TAAAGCTTTAATTTGGTTTGGATCCCATGCCCATGACCTGCCAGCTG
11610 27	ATTAGTGAAAA 11730	TTGGATCCCAT
11600	ACCTTTGAAT 11720	TTAATTTGGT
11590	A GAAATGAAA 11710	TTCTAAAGCT
1570 11580 11590 11600 11610 11610 11620 11630 11640	CCACGTAGGGA 11700	6CATTTT65C1
11570	TT GC AT ACCG	AASCAACACC
11560	AAGTCTTGAA 11689	agat tta a a G
11559	FAAACTAAAACA 11679	TC A A A A C C S A C
115.0	GTATETGTCTESAGGTGTAGTAAACTAAAECAAGTCTTGAATTGCAT 11659 11063 11679 11689	C A TC A A C A G CT
35 (1153) 11540 11559 11560 11	6TATATGTCT2 11650	15 A T 46C T T T (

FIG. 7k

		•					FIG. 8(a)
min. /	E-mag a	·					
-	- 1	0.000			ECOR1		GAATTC
, G.	₹3G	\$0.002	\$		HINF1		, GAATC
	33	0.003			MB011	N.	TCTTC
* 1		0.004		•	ALU1		AGCT
	48	0.004	3	•	DDE1	\$	CTGAG
		0.004	647		MNL1 ·		GAGG
		0.007			MNL1		CCTC
		800.0	5.		MST1		TGCGCA.
	95	0.008	i.		HHA1	0	GCGC
	112	0.009			MB01		GATC
•	120	0.010	‡.	•	98V1	•	GCAGC
	120	0.010	•		FNU4H1	1	GCAGC
	123	0.010		•	BBV1	•	GCAGC
	123	0.010			FNU4H1		GCAGC
	134	0.011	•		DDE1		CTGAG
	148	0.012	· .		HPH1	•	GGTGA
	173	0.014			MNL1		GAGG
	1 9 1	0.016			DDE1		CTTAG
	204	0.017			HINF1		GAATC
	247	0.021			SPH1	•	GC ATG C
	265	0.022		•	ALU1		AGCT GCTGC
	266	0.022		•	88V1		GCTGC
	266	0.022	.;		FNU4H1		GAACACTTTC
	305	0.026	7		XMN1 Alu1		AGCT
	376	0.032	â	• •	MNL1		GAGG
	417	0.035		•	STU1		AGGCCT
•	425	0.036			HAE111		GGCC
•	426	0.036			RSA1		STAC
• •	405	0.041			0051		CTTAG
	488 517	0.043	•		ALU1		AGCT
	523	0.044			ALU1		AGCT
	263	. 0.044				,	g ccrc
•	559	0.047			MNL1		₹ cctc
	578	0.049			RSA1		GTAC
	590	0.050	*		DDE1	-1	CTAAG
	621	0.052			ALU1		AGCT
	652	0.055			HINF1		GATTC
_	732	0.062			HIND111		AAGCTT
	733	0.062			ALU1		AGCT
	781	0.066			MB011		GAAGA
	788	0.066			MNL1		GAGG
	816	0.069			MNL1		GAGG
					•		

		FIG. 8(b)
818 0.069	FOK1	GGATG
898 0.076	MNL1	CCTC
898 0.076	MST11	CCTCAGG
899 0.076	DDE1	CTCAG CTGAG
913 0.077	DDE1	GGTGA
929 0.078 976 0.082	TAQ1	TCGA
1027 0.086	RSA1	GTAC
1032 0.087	MNL1	GAGG
1054 0.039	MNL1	CCTC
▶ 1072 0.090	HIND111	AAGCTT
1073 0.090	ALU1	AGCT
1099 0.092	98V1	GCAGC
1099 0.092	FNU4H1	GCAGC
1101 0.093	ALU1	AGCT
1138 0.096	MNL1	GAGG
1145 7.096	HINC11	GTTGAC
1150 0.097	FOK1 ALU1	CATCC AGCT
1161 0.098	HPH1	TCACC
1167 0.098 1193 0.100	HPH1	GGTGA
1198 0.101	ALU1	AGCT
1200 0.101	DDE1	CTG-AG
1204 0.101	MB011	GAAGA
1226 0.103	MNL1	GACG .
-12840.108	DDE1	CTGAG
1286 0.108	MNL1	GAGG
1323 0.111	RS41	GTAC
1365 0.115	BBV1	GCTGC
1365 0.115	FNU4H1	GCTGC
1370 0.115	XBA1	TCTAGA
1424 0.120	DDE1	CTAAG
1427 0.120	ALU1 RSA1	AGCT GTAC
1449 0.122 1603 0.135	ALU1	AGCT
1626 0.137	ACC1	GTATAC
14.633_00:13.7	HHINC11	GGT TAAC
10.10==18551/21-357	HPTMTEMELT	GITAMAGALLAL
7670 0.741	MNL7	GALL
1672 0.141	HAE111	GGCC
1685 0.142	FOK1	GGATG
1759 0.148	HINF1	GATTC
1766 0.149	MNL1	GAGG
1841 0.155	SAU961	GGGCC
1842 0.155	HAE111	GGCC

1855 0.156 DDE1 CTTAG 1884 0.159 MB011 TCTTC 1901 0.160 AVA11 GGACC 1901 0.160 SAU961 GGACC 1939 0.163 MNL1 CCTC 1940 0.163 DDE1 CTCAG	*			in in the second	FIG. 8(c)
1884 0.159 MB011 TCTTC 1901 0.160 AVA11 GGACC 1901 0.160 SAU961 GGACC 1939 0.163 MNL1 CCTC	1855 0.156		DDE1		-
1901 0.160 AVA11 GGACC 1901 0.160 SAU961 GGACC 1939 0.163 MNL1 CCTC			MB011		· ·
1901 0.160 SAU961 GGACC 1939 0.163 MNL1 CCTC			AVA11	المناجع المسج	
1939 0.163 MNL1 CCTC			SAU961		
CTCAG			MNL1		
	1940 0.163	•	DD 51		<u>CTC</u> AG

1947	0.164	_ ALU1	AGCT
1965	0.165	HAE111	GGCC
1965	0.165	SAU961	GGCCC
203C	0 171	RSA1	GTAC
2081	0 175	RSA1	GTAC
2097	0.177	· HGA1	GACGC
21.0	0.178	4LU1	AGCT
2112	0.178	55E1	CTCAG
2116	G.178	RSA1	GTAC
2128	0.179	MB01	GATC
2141	0.180	MNL1	CCTC
2147	0.181	MNL1	CCTC
2150	0.181	FOK1	CATCC
2158	0.132	MNL1	CCTC
2161	0.182	MNL1	CCTC
2165	0.182	MNL1	CCTC
2171	0.183	ACC1	GTAGAC
2174	0.183	HINF1	GACTC
2222	0.187	DDE1	CTTAG
2225	0.187	ALU1	AGCT
2248	0.189	PST1	CTGCAG
2282	0.192	MST11	CCTAAGG
2283	0.192	DDE1	CTAAG
2287	0.193	FOKI	GGATG
2296	0.193	MNL1	CCTC
2301	0.194	ALU1	AGCT
2349	0.198	9 9 V 1	GCTGC
2349	0.198	FNU4H1	GCTGC
2422	0.204	HINF1	GATTC
2468	0.208	HINF1	GATTC
2483	0.209	BSTE11	GGTAACC
. 2503	0.211	ALU1	AGCT
25 2 4	0.212	XBA1	TCTAGA
2534	0.213	DOE1	CTAAG
			•

					FIG. 8(d)
	3450	0 22/	RSA1		GTAC
	2658	0.224	SFNA1	:	GCATC
į.	2678	0.225	HINF1		GAGTC
	2726	0.230	HINC11		GTCAAC
	2728	0.230	•		GATTC
	.27.70	0.233	HINF1		GACGC
į	2807	0.236	HGA1		
	2811	0.237	DDE1	, ,	CTTAG
,	2965	0.250	HINF1		GATTC
	2984	0.251	AVA11	•.	GGTCC .
,	2984	0.251	SAU961		GGTCC
•	3012	0.254	MNL1	•	GAGG
,	3024	0.255	HINF1		GATTC
	3032	0.255	ALU1	•	AGCT
	3048	0.257	NDE1	.· 	CATATG
	3090	0.260	MNL1	, · · · · · · · · · · · · · · · · · · ·	GAGG
	3093	0.260	48011	•	GAAGA
	7 06	0.262	RSA1		GTAC
	3141	0.264	TAQ1		TCGA
	3168	0.267	RSA1		GTAC
	3193	0.269	MBO1		GATC
•	3213	0.271	HGIA1		GTGCTC
	3216	0.271	0051	•	CTCAG
	3220	0.271	MB011		GAAGA
	3234	0.272	RSA1		GTAC
	3263	0.275	MNL1	•	GAGG
	3333	0.231	NDE1		CATATG "
	3412	0.287	BCL1		TGATCA
	• .	٠.			

3413	0.287	M801	GATC
3415	0.288	HPH1	TCACC
3457	0.291	· 50E1	CTAAG
3462	0.292	HINF1	GACTC
3489	0.294	TAQ1	TCGA
3522	0.297	ECOR5	GATATC
3585	0.302	RSA1	GTAC
→ 3624	0.305	BGL11	AGATCT
36 2 5	0.305	. MB01	GATC
3638	0.306	MB 01	GATC
3689	0.311	HPH1	TCACC
3792	0.319	ALU1	AGCT V
	•		

: "		U	FIG. 8(e)
79/7	0.326	RSA1	GTAC
	0.324	oRSA1	GTAC
3905	0.327	BSTN1	CCAGG
3970 3970	0.334	SCRF1	CCAGG
		BSTE11	GGTAACC
3979	0.335	MNL1	GAGG
4016	0.338	SFNA1	GCATC .
4022	0.339	MB011	TCTTC
4025	0.368	HINF1	GAGTC
4368	0.369	RSA1	GTAC
4410	0.371	SFNA1	GATGC
4469	0.376	SFNA1	" GATGL
4520	0.381	RSA1	GTAC
45 2 3		DDE1	CTGAG
4525	0.381	MNL1	GAGG
4529	0.381	ECOR5	GATATC
4533	0.382	TAG1	TCGA
4058	0.392	HINF1	GAATC
4695	0.395	ALU1	AGCT
4719	0.397	XBA1	TCTAGA
4727	0.398	SFNA1	GCATC
4769	0.402	ECOR1	∀GAATTC
4769	0.402	XMN1	GAATTCTTTC
4778	0.402	DDE1	CTGAG
4780	0.403	HINF1	GAGTC
4848	0.408	NDE1	CATATG
4961	0.418	HINF1	GATTC
4933	0.420	DDE1	CTGAG
5020	0.423	ALU1	AGCT
50 2 2	0.423	DDE1	CTGAG
5049	0.425	HINF1	GATTC
5053	0.426	HP411	CCGG
5085	0.428	3 C L 1	TGATCA
.5086	0.428	MB01	GATC
→ 5157	0.434	PVU11	CAGCTG
5158	0.434	ALU1	AGCT
5225	0.440	ACC1	GTAGAC
5258	0.443	PST1	CTGCAG
5285	0.445	MNL1	GAGG
5339	0.450	ECOR5	GATATC
5355	0.451	RSA1	GTAC
53,67	0.452	HGIA1	GTGCAC
5394	0.454	RSA1	GTAC
5402	0.455	DDE1	CTCAG
5414	0.456	, BSTN1	CCAGG
	•		

FIG.	81	(f)
L TG.	0	

5421	0.456	MB011	GAAGA
_	0.459.	MB01	GATC
	0.459	ALU1	AGCT
		?	
	·•		
* .		7	:
5481	0.462	FNU4H1	GCGGC
5490		MNL1	GAGC
	0.468	ALU1	AGCT
5562		DDE1	CTGAG
	0.474	XMN1	GAAAGTATTC
	0.476	FOK1	GGATG
•	0.476	HINF1	GAGTC
•	0.478	PST1	CTGCAG
	0.478	BBV1	GCAGC
	0.478	FNU4H1	GCAGC
• •	0.485	BSTN1	CCTGG
•	0.485	SCRF1	CCTGG
	0.485	SAU961	GGGCC
_	0.485	HAE111	GGCC
	0.485	BSTN1	CCA GG
	0.485	SCRF1	CCAGG
	0.487	MNL1	CCTC
	0.490	ECOR5	GATATC
	0.490	HAE111	GGCC
	0.492	88V1"	GCTGC
		FNU4H1	GCTGC
	0.492	PST1	CTGCAG
	0.494	BAL1	TGGCCA
-	0.494	HAE111	GGCC
	0.495	SAU961	GGGCC
	0.495	HAE111	GGCC
		SAL1	TGGCCA
	0.496	HAE111	GGCC
	0.496	MNL1	GAGG
	0.497	STU1	AGGCCT
	0.497	HAE111	GGCC
	0.497 .	ALU1	AGCT
	0.499	MB011	GAAGA
	0.501	HINF1	GAATC
	0.501	DDE1	CTAAG
	0.502	SAU961	GGGCC
5971	0.503	380701	

			FIG. 8(g)
÷,		HAE111	GGCC
5972	0.503	· · · · · · · · · · · · · · · · · · ·	TCTTC
5987	0.504	MB 011	CCTGG
5994	0.505	BSTN1	CCTGG
5994	0.505	SCRF1	TCTTC
6000	0.505	48011	AGCT
6021	0.507	ALU1	
6026	0.507	ACC1	GTCTAC
6037	0.503	MNL1	GAGG
6121	0.515	ALU1	AGCT
6139	0.517	MB011	TCTTC
6177	0.520	MNL1	CCTC
6211	0.523	0051	CTTAG
6214	0.523	ALU1	AGCT
6233	0.525	HAE111	GGCC
-6248	0.526	HIND111	AAGCTT
6249	0.526	ALU1	AGCT
6275	0.528	AVA11	GGTCC
6275	0.528	SAU961	GGTCC
6305	0.531	RSA1	GTAC
6361	0.536	MB011	TCTTC
6370	0.537	BBV1	GCAGC
6379	0.537	FNU4H1	GCAGC
-> 6380	0.537	PVU11	CAGCTG
6381	0.537	ALU1	AGCT
6558	0.552	ΔVΑ11	GGTCC
	•		
		•	t
		•	•
			•
6558	0.552	SAU961	GGTCC
6561	0.553	BSTN1	CCTGG
6561	0.553	SCRF1	CCTGG
0,01	· • • • • • • • • • • • • • • • • • • •		CCTCA

6558	0.552	SAU961	GGTCC
6561	0.553	BSTN1	CCTGG
6561	0.553	SCRF1	CCTGG
		HPH1	GGTGA
6564	0.553		_
6629	0.558	HINF1	GAATC
6639	0.559	MBO1	GATC
	0.562	HINF1	GAATC
6674	• • • •		, -
6677	0.562	XBA1	TCTAGA
6683	0.563	STU1	AGGCCT
6684	0.563	HAE111	GGCC
		· · · · · · · · · · · · · · · · · · ·	₹ GC A GC
6722	0.566	9BV1	
6722	0.566	FNU4H1	GCAGC
	0.570	SFNA1	GCATC
6767		_	
6793	0.572	FOK1	GGATG
6848	0.577	HINF1	GACTC
0040	U • J · /	17 - 111 1	

FIG. 8(h)

- Z			
6874	0.579	HINF1	GATTC
6911		ECOR1	GAATTC
6916	0.582	HPA11	CCGG
6984	0.588	ALU1	AGCT
6991	0.589	HINF1	GACTC
7028	0.592	SAU961	GGGCC
7029	0.592	HAE111	GGCC
7027	0.593	DDE1	CTCAG
	0.594	FOK1	GGATG
7052	0.594	S AU 961	GGGCC
7056		HAE111	GGCC
7057	0.594	MNL1	CCTC
7059	0.594	•	TCTTC
7124	0.600	MB011	GAAGA
7155	0.603	MB011	GAAGAGTTY
7155	0.603	XMN1	CTAAG
7179	0.605	DDE1	AGCT
7182	0.605	ALU1	
7185	0.605	. HPH1	TCACC
7194	0.606	DDE1	CTGAG
719 ć	0.606	MNL1	GAGG
7237	0.509	ALU1	AGCT
7293	0.614	AVA1	CTCGGG
731 C	0616	MB011 .	GAAGA
7313	0.616	SFNA1	GATGC
7322	0.617	estn1	CCAGG
7322	0.617	SCRF1	CCAGG
7343	0.618	RSA1	GTAC
7373	0.621	HGIA1	GAGCTC
7373	0.621	SAC1	GAGCTC
7374	0.621	· ALU1	AGCT
7376	0.621	DDE1	CTCAG
> 7378	0.621	PVU11	CAGCTG
7379	0.621	ALU1	AGCT
7394	0.623	HAE111	3G C C
7396	0.623	= BSTN1	CCAGG
7396	0.623	SCRF1	CCAGG
7408	0.624	DDE1	CTGAG
7410	0.624	MML1	GAGG
7438	0.626	FOK1	GGATG
7485	0.630	STU1	AGGCCT
7480	0.630	HAE111	GGCC
7488		MNL1	CCTC
7507	0.632	HPH1	GGTGA
7516	0.633	MNL1	GAGG
7529	0.634	ALU1	AGCT
7547	0.636	MRO11	GAAGA
11347	0.030	BNUTT	UAAUA

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			•
7580	0.638	HINF1	GATTC
7599	0.040	'HINC11	GTCAAC
7619	0.642	MB011	GAAGA
7634	0.643	RSA1 ·	GTAC
7637	0.643	ODE1	CTCAG
7659	0.545	ALU1	AGCT
7681	0.647	нрн1	GGTGA
7705	0.649	DDE1	CTAAG
7745	0.652	HINF1	GACTC
7753	0.553	MNL1	GAGG
7802	0.657	HINF1	GAGTC
7809	0.658	MB01	GATC
794 G	0.669	BSTN1	CCTGG
7940	0.669	SCRF1。	CCTGG
7963	0.671	MNL1	CCTC
7989	0.673	ALU1	AGCT
8002	0.674	HINF1 ~	GACTC
3013	0:675	HGIA1	GTGCTC
8021	0.675	`· ALU1	AGCT
8031	0.676	MNL1	GA G G
8035	0.677	DDE1	CTGAG
8037	0.577	MNL1	GAGG
8046	0.678	HINF1	GAATC
8049	0.678	HPH1	TCACC
8053	0.678	- DDE 1	CTGAG
3058	0.679	BSTN1	CCTGG
8058	0.679	SCRF1	CCTGG
8067	0.579	. TAQ1	TCGA
8069	0.680	MNL1	GAGG
.8072	0.680	B8V1	GCTGC
8072	0.680	FNU4H1	GCTGC
3073	0.680	PST1	CTGCAG
8086	0.681	BCL1	TGATCA
8087	0.681	MB01	GATC
3109	0.683	0051	CTGAG
8160	0.687	· HAE111	GGCC
816C	0.687	SAU961	GGCCC
8190	0.690	HPA11 .	CCGG

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F	IG	8	(j)

8190	0.690	NCI1 CCGGG	
· 8190		SCRF1 . CCGGG	
8220	0.692	RSA1 GTAC	
8233	0.693	AVA1 CCCGGG	
8233	0.693	NCI1 CCCGG	
18233	0.693.	SCRF1 CCCGG	
8233	0.693	SMA1 CCCGGG	
3234	0.693	HPA11 CCGG	
8234	0.693	NCI1 CCGGG	
8234	0.693	SCRF1 CCGGG	
8238	0.694	HGIA1 GTGCTC	
8243	0.694	PST1 CTGCAG	
8282	0.697	NDE1 CATATG	
8357	0.704	DDE1 CTTAG	
8366	0.705	PVU11 -/ CAGCTG	
8367	0.705	ALU1 AGCT	
8376	0.705	DDE1 CTAAG	
3382	0.706	HINF1 GATTC	
8396	0.707	MBO11 GAAGA	
841 G	0.708	MNL1 CCTC	
8417	0.709	HAE111 GGCC	
. 3417	0.709	SAU961 GGCCC	
8423	0.709	MNL1 CCTC	2,
	•	,	

8428	0710	BSTN1	CCAGG
8428	0.710	SCRF1	CCAGG
8440	0.711	BSTN1	.CCAGG
8440	0.711	SCRF1	CCAGG
3443	0.711	FOK1	GGATG
3447	0.711	AVA11	GGTCC
8447	0.711	SAU961	GGTCC
8477	0.714	BSTE11	GGTAACC
8492	0.715	NDE1	CATATG
3643	0.728	PST1	CTGCAG
9221	0.777	MBO1	GATC
9263	0.780	MNL1	CCTC
9266	0.780	MNL1	· CCTC
9294	0.783	MNL1	GAGG
9335	0.786	FOK1	CATCC
9350	0.787	MB 011	TCTTC

FIG. 8(k)

16 1 4 4 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	•		
9353	0.788	MB011	TCTTC
9394	0.791	BSTN1	CCTGG /
9394	0.791	SCRF1	CCTGG
9400		MNL1	CCTC
95 5 C	0.804	MB01	GATC
9571	0.804	MB011	TCTTC
9600		HGIA1	GTGCTC
9603		DDE1	CTCAG
→ 9614	0.810		GGATCC
9615	0.810	MB01	GATC
9626	0.811	BSTN1	CCAGG
9626	0.811	SCRF1	CCAGG
9641	0.812		AGCT
9643	0.812	DOE1	CTAAG
9647		MB011	GAAGA
9676			GATTC
9681	0.816	MB01	GATC
- 96 9 4	_	FOK1	CATCC
9697		BSTN1	CCTGG
9697		SCRF1	CCTGG
9723		MB011	TCTTC
9747		NCI1	CCCGG
9747		SCRF1	CCCGG
	0.821	HPA11	CCGG
9762	0.822	HAE11	GGCGCC
9762		* NART	GGCGCC
9763		° HHA1	GCGC
9777		ALU1	AGCT
9787		MNL1	GAGG
9791		DDE1	CTGAG
9793		MNL1	GAGG
9814	0.826	HPA11	CCGG
9814	0.826	NC I 1	CCGGG
39814	0.826	SCRF1	CCGGG
9819	0.827	•	GAGG
9826	0.828	ALU1	AGCT
9843	0.829	MBO1	GATC
¥9864	0.831	BSTN1	CCTGG
9864	0.831	SCRF1	CCTGG
9881	0.832	-HINF1	GACTC
10246	0.863	HINF1	GATTC
10279	0.866	ALU1	AGCT
10281	0.866	0051	CTGAG
10284	0.866	ALU1	AGCT
10310		TTH1111	GACCCTGTC
		•	परिहार र

FIG. 8(L)

		•		
	10336	0.870	MNL1	CCTC
	10347	0.371	MNL1	CCTC
,	10351	0.872	FOK1	CATCC
	10455	0.880	HI1F1	GAATC
	10463	0.881	MNL1	CCTC
	10473	0.882	FOK1	GGATG
	10477	0.882	SAU961	eeecc
	10478	0.332	HAE111	GGCC
	10482	0.583	ALU1	AGCT
	10505	0.885	PST1	CTGCAG
	10512	0.885	MNL1	GAGG
	10536	0.387	M301	GATC
	10543	0.888	PST1	CTGCAG
	10545	0.838	53V1	GCAGC
	10545	J.888.	FNU4H1	GCAGC
	10563	0.390	ODE1	CTAAG
	10568	0.890	SFNA1	GCATC
	10539	0.392	PVU11	CAGCTG
	10590	0.892	ALU1	AG C T
	10605	0.393	HPH1	GGTGA
	10625	0.895	ALU1	AGCT
	10656	0.897	HPH1	TCACC
	10685	0.900	SFNA1	GATSC
	10093	0.901	MB011	TCTTC
	10733	0.904	BSTN1	CCAGG
	10733	0.904	SCRF.1	CCAGG
	10751	0.905	ect1	TGATCA
	10752	0.905	ME01	GATC
	1075C	0.906	HPH1	GGTGA
	10763	0.906	MB011	GAAGA
	10779	0.908	M50.11	GAAGA
	10865	0.915	нрч1	GGTGA
	10869	0.915	ALU1	AGCT
	10099	0.918	MB011	GAAGA
	10925	0.920	HPH1	GGTGA
	1095G	0.922	HINF1	GATTC
	10958	0.923	MNL1	CCTC
	11015	0.928	93V1	GCAGÇ

FIG. 8(m)

	₩.		
-11015-	0.928	FNU4H1	GCAGC
11061	0.932	HINC11	GTTGAC
11073	0.933	ALU1	AGCT
		FNU4H1	GCGGC
11095	0.934	HPH1	TCACC
11132	0.938		CCTGG
11135	2.	BSTN1	CCTGG
11135	0.938	SCRF1	•
11137	0.938	BAL1	TGGCCA
11138	0.938	HAE111	GGCC
11145	0.939	MBO1	GATC
e-11157	0.940	DDE1	CTAAG
11170	0.941	SAMH1	GGATCC
11171	0.941	MBO1	GATC
11181	0.942	· ALU1	AGCT
11256	0.948	BSTN1	CCAGG
11256	0.948	SCRF1	CCAGG
11265	0.949	нрн1	TCACC
	0.949	MNL1	CCTC
11268		DDE1	CTCAG
1126	0.949		AGCT
11272	0.949	ALU1	CCAGG
11278	0.950	BSTN1	
11278	0.950	SCRF1	CCAGG
11300	0.952	2 B V 1	GC A G C
		• • · · ·	

	·		
1130G	0.952	FNU4H1	GCAGC
11303	0.952	FNU4H1	GCCGC
11314	0.953	NRU1	TCGCGA
1.1315	0.953	FNUD11	CGCG
11324	0.954	ALU1	AGCT
1133G	0.954	BSTN1	CCAGG
11330	0.954	SCRF1	CCAGG
11349	0.956	HPA11	CCGG
11356	0.956	HAE11	GGCGCT
11357	0.956	HHA1	GCGC
11367	0.957	FOK1	CATCC
11381	0.958	MNL1	· CCTC
11428	0.962	FNUD11	CGCG
11429	0.963	нна1	GCGC
11447		HPA11	CCGG
11464	0.965	MNL1	GAGG
11404		• • • •	•

FIG. 8(n)

11466 0.966 HAE111 GGCC 11478 0.967 MNL1 GAGG 11481 0.967 RSA1 GTAC 11494 0.968 MNL1 CCTC 11497 0.968 BSTN1 CCAGG 1150C 0.968 HAE111 GGCC 11500 0.968 SAU961 GGCCC 11500 0.969 HAE111 GCCG 11505 0.969 HHA1 GCGC 11515 0.970 DDE1 CTCAG 11515 0.970 DDE1 CTCAG 11515 0.970 HGIA1 GAGCTC 11519 0.970 SAC1 GAGCTC 11519 0.970 ALU1 AGCT 11533 0.971 AVA1 CTCGGG 11557 0.973 MB011 GAAGA 11560 0.974 XMN1 GAAATACTTC 11581 0.975 MNL1 GAGG 11580 0.976 ALU1 AGCT 11591 0.976 MNL1 GAGG 11648 0.981 XBA1 TCTAGA 11652 0.991 MNL1 GAGG 11648 0.981 XBA1 TCTAGA 11650 0.994 ALU1 AGCT 11778 0.992 ALU1 AGCT 11829 0.996 HIND111 AGCT 11828 0.996 HIND111 AGCT 11829 0.998 BAMH1 GGATCC 11846 0.998 BAMH1 GGATCC 11868 0.999 PVU11 CAGCTG 11868 0.999 PVU11 CAGCTG 11868 0.999 PVU11 CAGCTG 11869 1.000 ALU1 AGCT				
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FIG. 9(b)

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さん 一大きな かんしょうけん こうかんしょう

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. H - Gr Gr C Gr C G C L C G C L L	7

AAACIEGTETTCIEGTTCAAA 2770

33/35 Best Available Copy

Oligo N3 5' GATCCAGCTGA 3'
Oligo N4 3' GTCGACTTCGA 5

Fig. 10

Eco RI

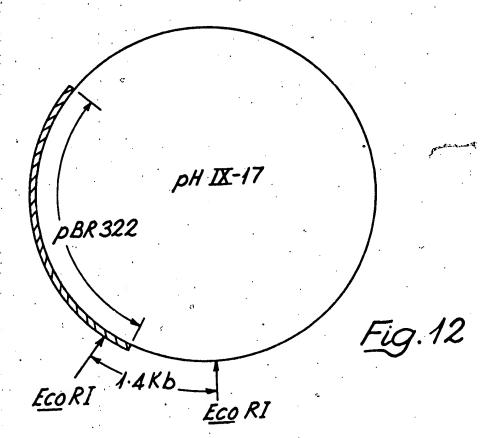
10 20 1 30 1 40 50

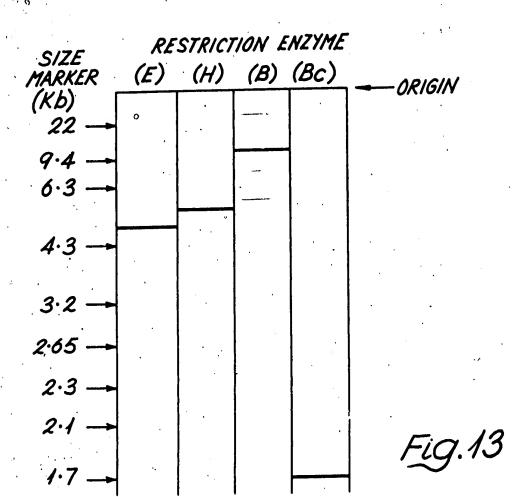
5' GAA TTCTCATGTT TGACAGCTTA TCATCGATAA GCTTCAGCTG GATCCTCTAC

60

GCCGGACGCA 3'

Fig. 11





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